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MASTER

RADIOBIOLOGY OF PIONS AT LAMPF

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RADIOBIOLOGY OF PIONS AT LAMPF

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ABSTRACT

Recent radiobiology data for pion beams used in therapy are presented. The biological systems used were cultured cells suspended in gelatin and intestinal crypt assay. The importance of fast neutrons from pion stars in large treatment volumes is discussed.

The data for compensating the depth dose distribution to produce uniform cell killing across the peak region are presented. The changes in biological effectiveness with peak width for pion beams (unlike heavy ions) are small because of fast neutron contribution from pion stars. The need for innovative radiobiology programs to guide high-LET radiotherapy is discussed.

INTRODUCTION

The physical aspects of pions differ from the rest of heavy charged particles in some respects. For pions, the increase in LET in the peak region due to Bragg ionization characteristics is radiobiologically insignificant. The high-LET component in the pion stopping region is from pion stars. The relative contributions of charged particles and fast neutrons from pion stars depend on the pion stopping volume. The contribution of fast neutrons in small stopping volumes is small compared to charged particles. However, with increasing pion stopping volume, the role of fast neutrons becomes important. This is illustrated in the schematic diagram shown in Fig. 1 (1). The decrease in high-LET components due to charged particles from pion stars with increasing peak width of pions is partly compensated by the increase in contribution by fast neutrons from pion stars. These physical considerations could mean that the radiobiological effect of pions may depend not only on peak width but also on beam size.

Secondly, the differences in biological effectiveness of pions of different peak widths will be small compared to heavy ions.

RESULTS

1. Cultured Cells

When the narrow Bragg peak is broadened to cover large treatment volumes, the distal side of the peak is more effective than the proximal peak because of the changes in LET across the peak. Cultured hamster cells (V79) suspended in gelatin (3) were used to study the beam characteristics of pion beams used in therapy (2). Figure 2 shows cell survival curves at three positions across a 14-cm wide peak. These differences in cell killing need to be appropriately compensated in order to produce uniform cell killing in the region of interest. Figure 3 shows such a dose distribution along with cell-killing data as a function of depth. Most of the pion beams used in therapy were verified for uniform cell killing across the peak region.

Figure 4 shows cell survival curves at the peak center of the pion beams of peak width 6, 10 and 14 cm. The biological effectiveness is found to decrease slightly with increasing peak width.

Our results from cultured cell experiments are consistent with the results from Vancouver reported in this workshop.

2. Intestinal Crypt Cells

The biological effects of pion therapy beams are also measured using mouse jejunum for pion beams used in therapy (5-7). Since there are no differences between abdominal irradiation and whole-body irradiation in this system, there is no need to use any additional collimation that could change the beam quality. Single and four fractions were used. The fraction number was dictated by the beam availability. The objectives of this study are to: 1) verify the uniformity of cell killing across the range-modulated pion beam, 2) measure the

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difference in biological effectiveness between beams of different peak width (equal field size), and 3) study the neutron effect of beams of 8-cm peak width but of different field sizes.

The cell killing across the range modulated pion beam of 14-cm peak width at the proximal, mid and distal peak positions was found to be uniform, consistent with cultured cell experiments. Figure 5 shows cell survival of intestinal crypts for pion beams of 6- and 14-cm peak width at the peak center. Consistent with cultured cell experiments, the differences are small and there is also a suggestion that 6-cm peak width is slightly more effective than 14-cm peak width beam at low doses.

To study the effect of neutron contribution differences between pion beams of different stopping volumes but of the same peak width, two beams of peak width 8 cm, but of field sizes (7.5 x 7.5 cm) and (20 x 20 cm) were tested using the mouse jejunum for one and four fractions at the mid peak positions. The dose rate was 0.12 Gy/min for large beam and 0.6 Gy/min for the small beam. The results are shown in Fig. 6. The data indicate that the biological effect is greater for the large beam compared to the small beam when four fractions were used despite the fact that the dose rate for the large beam is considerably lower than that for the small beam. However, no difference was seen when single doses were used. Thus, it appears that in addition to the peak width, pion stopping volume also must be taken into consideration because of fast neutron contribution from pion stars. Since treatment of large tumor volumes often requires beams with larger peak widths, the neutron contributions tend to decrease the differences in biological effect for pion beams of different peak widths. These findings are consistent with the results of cultured cell experiments reported by Dr. Skarsgard in this workshop.

3. Late Effects

RBE measurements of late effects for pions in the past were made using narrow peak width (2-cm) because of limited dose rate. The RBE values of such beams may be different from beams used clinically. Recently, an extensive series of fractionated experiments (up to 20 fractions) has been conducted by Dr. van der Kogel for the late effects on the cervical spinal cord in rats and mouse lungs with a pion beam of 6-cm peak width. We expect to have the results within a few months. To address the question regarding possible differences in RBE for pions between acute and late effects, Dr. Tokita compiled the available data for narrow peak of pions for acute effects on mouse skin, mouse jejunum and for late effects on the mouse kidney, rat spinal cord, and rat colon. There is a suggestion that the slopes for late effects appear to be steeper compared to acute effects (6).

DISCUSSION

When pions were proposed, the importance of fast neutrons from pion stars was not recognized. For heavy charged particles, the RBE decreases and OER increases with increasing peak width. These changes for pion beams are rather small because of fast neutron contribution. The results from Los Alamos are consistent with the radiobiology data from Vancouver.

When high-LET particles were proposed for therapeutic use, the emphasis was placed mainly on the effect on tumor cells in hypoxic state and tumor cells in resistant phases of the cell cycle, but not on the late normal tissue tolerance in spite of earlier warnings by Stone (4). For lack of information regarding the optimum fractionation scheme for high-LET radiations, conventional fractionation schemes (using approximately 2 Gy X-ray equivalent doses per fraction) developed for X rays are being used for high-LET particles as well. Clinical experience from such fractionation schemes alone can not determine the potential

application of high-LET particles in therapy because cell killing by high-LET particles is less influenced by hypoxia and stage in the cell cycle. Also, since accumulation of sublethal damage is less important for high-LET particles, no advantage is obtained in sparing normal tissues from late effects when conventional fractionation schemes are used. Although, in the final analysis, clinical trials have to determine the potential role of high-LET particles, the role of radiobiology has to be much more than just determining the RBE at a dose per fraction currently used. With increasing power costs, it may not be possible to arrive at the answers by clinical trials alone. It is important to have an innovative radiobiology program to guide the therapy program in the selection of fractionation schemes by a detailed study of the tolerance of normal tissues for acute and late effects and the selection of tumors suitable for high-LET radiotherapy (e.g., slow-growing tumors).

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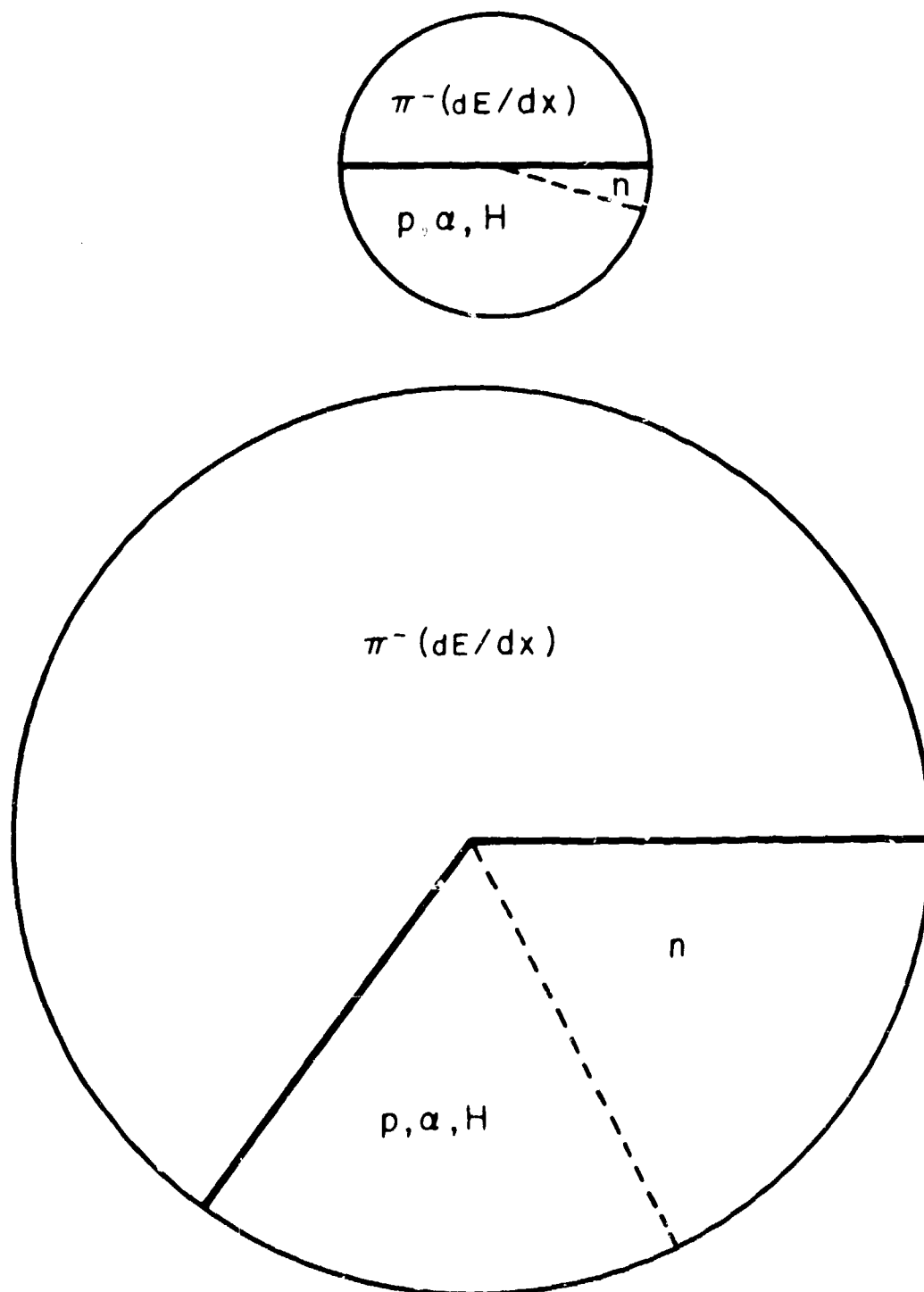
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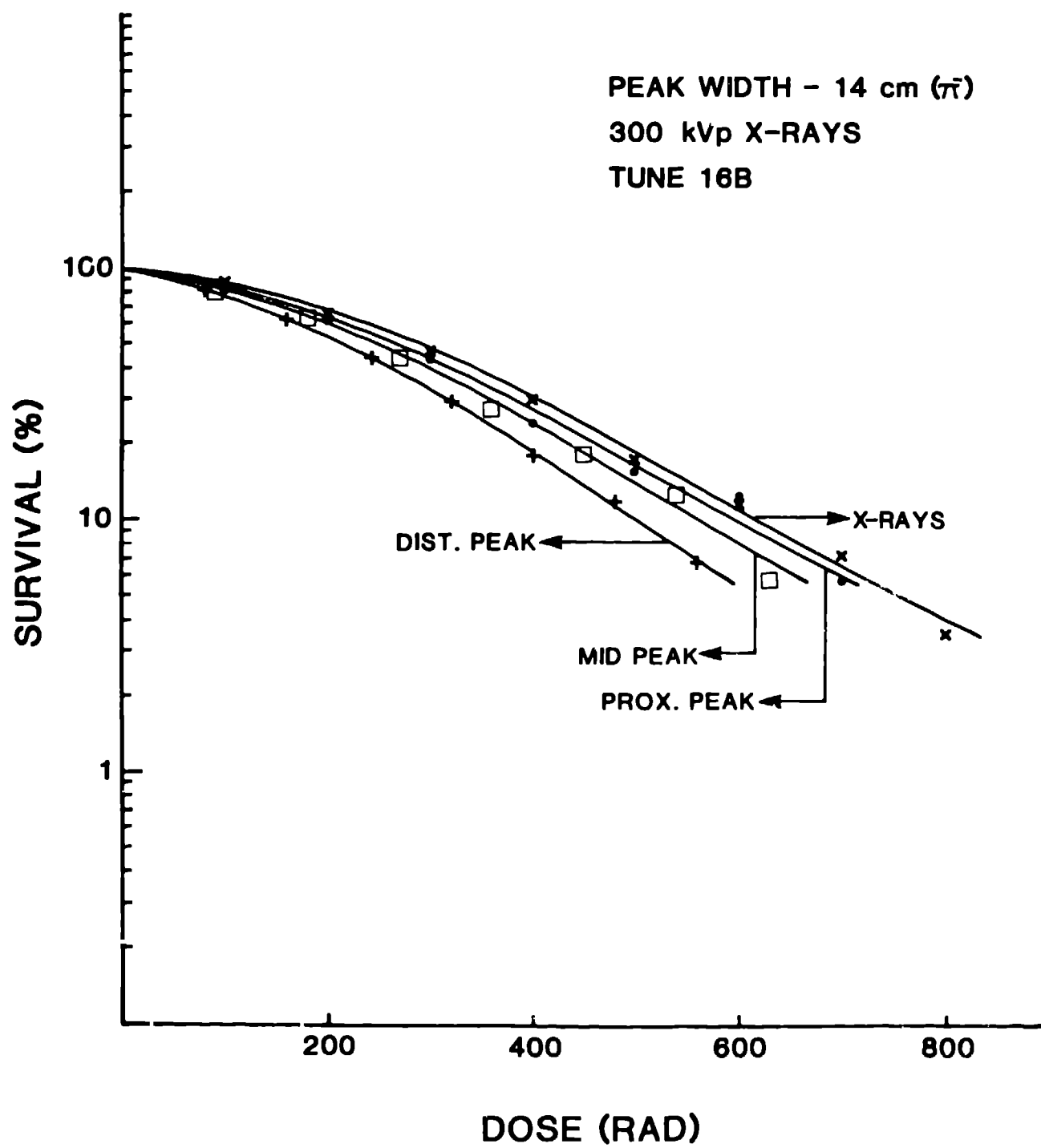
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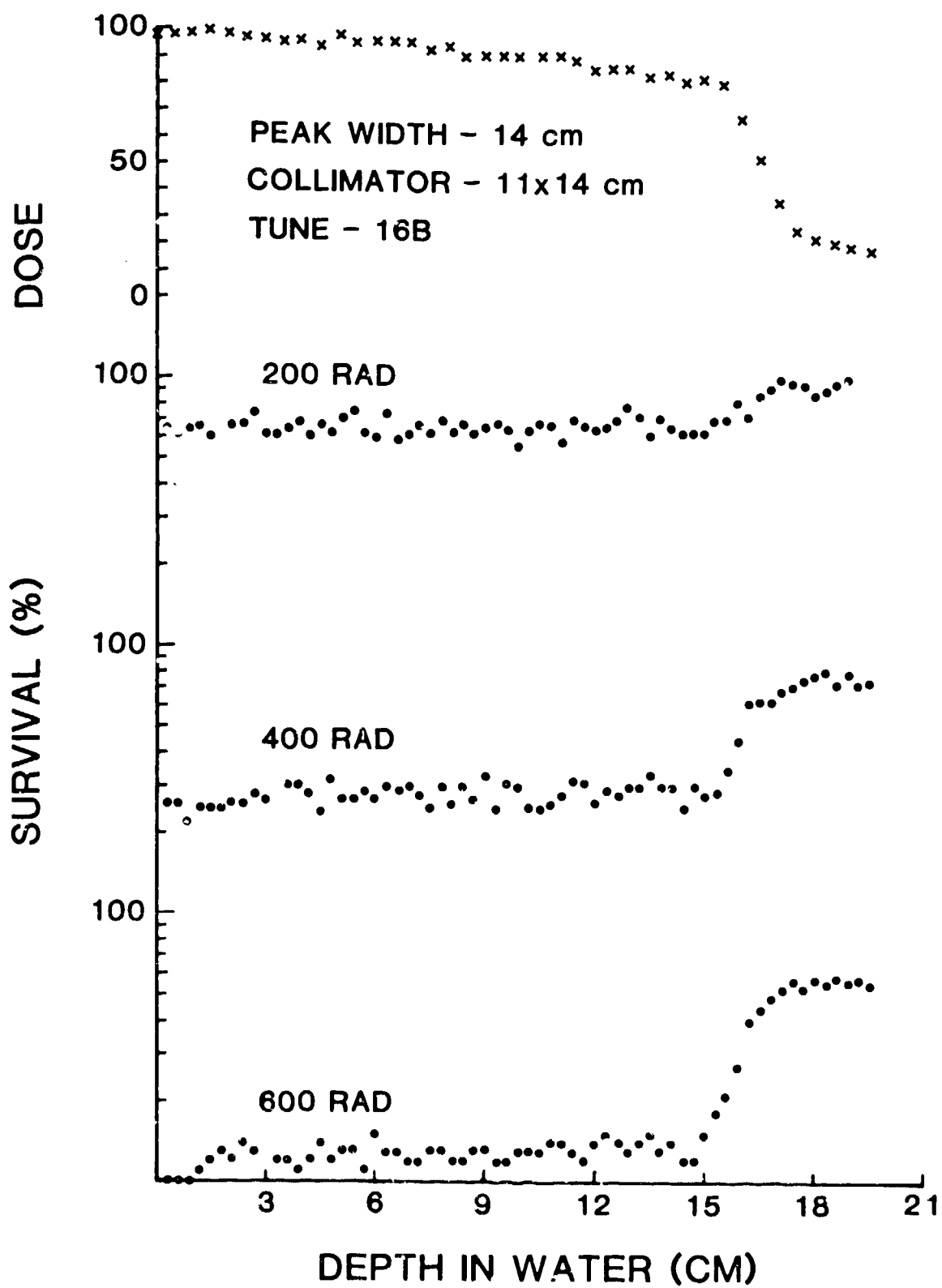
FIGURE LEGENDS

1. Schematic representation of doses deposited by pions in small (~ 0.2 Liter) and large (~ 1.5 Liter) volumes. The numbers used in this Figure are from Monte-Carlo calculations by Dr. J. J. Brenner (personal communication, June, 1981).
2. Cell survival curves at proximal-, mid-, and distal-positions of pion beam of peak width 14 cm and for 300 KVp X rays.
3. Depth dose distribution and cell survival as a function of depth for a pion beam of 14 cm peak width.
4. Cell survival curves for peak center position of peak widths 6 cm, 10 cm, and 14 cm and 300 KVp X rays.
5. Intestinal crypt cell survival curves at the mid peak position of the 14-cm (open squares) and 6-cm (closed squares) peak widths, but of equal size (11 cm x 14 cm).
6. Intestinal crypt cell survival curves for a pion beam of 8-cm peak width but of sizes 7.5 cm x 7.5 cm (small field) and 20 cm x 20 cm (large field) following 1 and 4 pion dose fractions.

DOSE DEPOSITION BY PIONS







PEAK WIDTH: 6, 10 & 14cm.
300 KVp X-RAYS
PEAK CENTER

